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Phosphorylation of p53 Protein in A549 Human Pulmonary Epithelial Cells Exposed to Asbestos Fibers

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Abbreviations: PIKK, phosphatidylinositol 3-kinase related kinase; DNA-PK, DNA-activated protein kinase; ATM, ataxia telangiectasia mutated; ERK, extracellular signal-regulated protein kinase; MAPK, mitogen-activated protein kinase; DMSO, dimethyl sulfoxide; DSBs, double-strand breaks.

Outline of manuscript section headers:

Abstract

We examined effects of asbestos exposure on the phosphorylation of p53 protein in human pulmonary epithelial type II cells (A549) which express wild-type p53. In cells exposed to two different types of asbestos, chrysotile (~1-6% iron content) and crocidolite (~27% iron content) fibers, at the doses of 1, 5 and 10 μg/cm^2 for 24 hr, the levels of p53 phosphorylated at Ser15 and p53 protein were correlated with the dose. On a per weight basis, chrysotile was more potent to induce Ser15 phosphorylation and accumulation of p53 protein than crocidolite. Following to the exposure to 10 μg/cm^2 chrysotile, the levels of p53 phosphorylated at Ser15 and p53 protein increased after 18 hr. Among serines in p53 protein immunoprecipitated from A549 cells treated with chrysotile, only Ser15 was phosphorylated markedly. In contrast, no clear phosphorylation was observed at Ser6, Ser9, Ser20, Ser37, Ser46 and Ser392. Blocking of extracellular signal-regulated protein kinase pathway with U0126 or inhibition of p38 activity with SB203580 did not suppress chrysotile-induced Ser15 phosphorylation. On the other hand, treatment with wortmannin, an inhibitor of DNA-activated protein kinase and ataxia telangiectasia mutated, suppressed both chrysotile-induced Ser15 phosphorylation and accumulation of p53 protein. Treatment with either catalase or N-acetylcysteine failed to suppress chrysotile-induced Ser15 phosphorylation, suggesting that reactive oxygen species do not seem to play a major role in the phosphorylation of p53 protein. The present results showed that asbestos, particularly chrysotile, induces phosphorylation of p53 protein at Ser15 in A549 cells depending on a DNA-damage signaling pathway.